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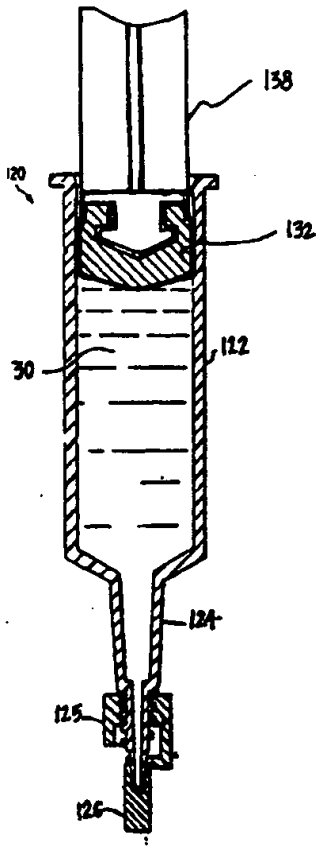
(54) Title: PRE-FILLED, STERILIZED SYRINGE AND METHOD OF MAKING

(57) Abstract

A pre-filled, sterile delivery apparatus (20) and the process for making the apparatus. The apparatus is in the form of a syringe having a liquid filled container (22) with a sealed nozzle (24) at one end and an opposite end sealed by a piston (32). The piston has an elastic body portion with a solid film lubricant outer layer (36) to facilitate sliding engagement of the piston with the interior wall of the container. The sealed assembly is sterilized to provide a sterile syringe having sterile contents. The solid film lubricant provides the piston with the sliding property while avoiding the use of silicone oils or the like which can contaminate the liquid contents. The piston undergoes sterilization while within the container without adverse effect, e.g., delamination. The disclosed process involves filling the syringe container with a desired fluid material, e.g., a contrast medium, sealing the container with the piston, and sterilizing the sealed assembly.



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PRE-FILLED, STERILIZED SYRINGE AND METHOD OF MAKING

Field of the Invention

This invention relates to prefilled sterile delivery apparatus containing various media such as fluids suitable for injection in the diagnosis and/or treatment of medical conditions and the method of manufacturing the same.

Description of the Prior Art

It is known in the prior art to form prefilled sterile glass syringes wherein the syringe parts are washed and sterilized prior to assembly and filling of the syringe. After filling, the syringe is sealed with a piston and the assembled syringe and its contents are autoclaved or otherwise treated to sterilize both the syringe and its contents.

It is also known to produce prefilled sterile plastic syringes by first removing contaminants from the syringe barrel, the piston, and the nozzle tip seal, and then placing the tip seal on the nozzle, filling the syringe with a desired quantity of liquid material, assembling the piston in the open end of the barrel, and autoclaving the sealed syringe to sterilize the syringe and its contents. For a disclosure of such techniques, see U.S. Patent N s. 4,628,969 and 4,718,463. While it was previously not known that such

plastic syringes would be able to withstand autoclaving, the above patents disclose that it is indeed possible to use such heat sterilization techniques on prefilled sealed plastic syringes without distortion of the barrel. The disclosed process may include, among other steps, maintaining a pressure on the outside surfaces of the filled syringe at least as great as the pressure of the syringe contents during autoclaving.

In manufacturing the prefilled syringes of the prior art discussed above, a layer of silicone lubricant is applied to the inner surface of the syringe barrel, the tip seal and the piston prior to filling and assembly of the syringe. This lubricant is used to provide the syringe barrel and piston with requisite sliding properties that allow smooth movement of the piston within the barrel with relatively little friction. However, the presence of the silicone lubricants in locations wherein the same come into contact with the injection fluids in the syringe presents a risk that particulates of the silicone lubricant will be incorporated in the injection fluid and injected with it.

Accordingly, it is an object of the present invention to provide a prefilled, sterile delivery apparatus and process for making the same in which the aforementioned problem is overcome.

Summary of the Invention

The present invention provides a prefilled, sterile delivery apparatus and process for making the same in which a satisfactory sliding relationship between the piston and syringe barrel is attained without possible entraining of silicone oil in the

injection fluid stored in the syringe and delivered therefrom.

Other features of the invention will be apparent from the following description of the preferred embodiments taken in conjunction with the accompanying drawings wherein:

Brief Description of the Drawings

FIG. 1 is a sectional view of a prefilled, sterile delivery apparatus embodying the present invention.

FIG. 2 is a sectional view of a prefilled, sterile delivery apparatus in the form of another embodiment of the present invention.

Detailed Description of the Preferred Embodiments

With reference to the embodiment of FIG. 1, a prefilled, sterile delivery apparatus in the form of a syringe indicated generally at 20 includes a container or barrel 22 having a delivery end in the form of a nozzle 24 and an open end 28 away from the nozzle 24. While the container 22 is shown as cylindrical, it will be recognized that such shape is exemplary only and that the container 22 can be of either a cylindrical or a non-cylindrical shape, e.g. triangular or square. The nozzle 24 is shown closed by a tip seal 26, but it will be recognized that any suitable means for closing the nozzle so as to seal the contents 30 within the syringe 20 is sufficient. The open end 28 of the container 22 is closed and sealed by a piston 32 to form a storage volume containing the fluid contents 30. The contents 30 can be any medicinal or diagnostic fluid material, including but not limited to contrast media. As used herein, the term fluid means a medical fluid and encompasses liquids, gases or combinations

thereof, comprising or containing pharmaceutical media. The piston can be operated by a handle 38 for expelling the contents 30 through the nozzle 24. The syringe parts are individually manufactured and the container 22 can be of any suitable material capable of withstanding applicable sterilization techniques, e.g. autoclaving. In the preferred embodiment, the container 22 is produced by a suitable plastic-forming process such as injection molding of a suitable polymer such as polypropylene, or a co-polymer of polypropylene and polyethylene. The tip seal 26 is likewise produced by injection molding a suitable elastomeric plastic or rubber material to the desired shape.

The piston 32 is formed by a piston body 34 having laminated thereto an outer solid film lubricant layer 36. In a preferred embodiment, the piston body 34 is formed of a resilient material such as rubber and the solid film lubricant layer is a tetrafluoroethylene resin. The piston 32 is similar in structure to the piston arrangement utilized in the unfilled syringe assembly disclosed in U.S. Patent Nos. 5,009,646 and 4,997,423.

A procedure for producing the piston is disclosed in the aforementioned patents and includes placing a film for lamination on the surface of a rubber sheet and then simultaneously subjecting the film and sheet to molding and laminating. Also disclosed in the referenced patents are various materials from which the piston body and solid film layer can be suitably manufactured. The piston body can be made, for example, of a rubber or elastic or resilient material including isoprene, butadiene, styrene-butadiene, ethylene-propylene, isoprene-isobutylene and nitrile rubbers. The solid film lubricant layer can be made,

for example, of a fluoro resin film including tetrafluoroethylene or ethylene-tetrafluoroethylene, and can also be made of a polyethylene resin.

The prefilled, sterile syringes of the prior art, which utilize a mist of silicone oil placed on the piston and barrel, are filled with fluid and then subjected to a rigorous sterilization process, e.g. an autoclaving process which typically involves placing the filled syringes in a steam/air autoclave operating at temperatures of about 125°C.

One of the severe limitations placed on the design of such prefilled and sterilized syringe assemblies is the requirement for withstanding the physically harsh conditions of the sterilization process, such as autoclaving. In this respect, it was previously not known that a piston having a structure comprising a piston body with an outer solid film lubricant layer disposed over the body could withstand such extreme environmental conditions associated with sterilization processes to which prefilled syringes are subjected without degradation of the mechanical integrity of the piston, such as, e.g. in the form of delamination of the solid film lubricant from the piston body, caused by drastically different coefficients of thermal expansion of the piston body, which is usually rubber, and the film lubricant, which is a tetrafluoroethylene or an ethylene-tetrafluoroethylene resin. As the syringe and its contents are sterilized by being heated in the autoclave, the solid film layer and the piston body are caused to expand at different rates and, in addition, transient temperature gradients will be present in the syringe as it is heated from its initial temperature to an equilibrium temperature. Such gradients cause temperature differentials between the

solid film lubricant outer layer and the piston body, this creating further delaminating forces. Any such degradation would, of course, adversely affect the sealing of the syringe barrel by the piston. It is of utmost importance that the integrity of the piston seal be maintained during the sterilization process and thereafter until the syringe is used.

Pursuant to the present invention it has been unexpectedly discovered that the prefilled, sterile syringe apparatus of the present invention can be subjected to a harsh sterilization process, e.g. autoclaving, without any mechanical degradation such as delamination of the piston body and film layer or other compromise of the sealing properties of the piston. It is thus possible in accordance with the present invention to produce a prefilled, sterile syringe 20 in which a proper sliding relationship between the piston 32 and the container 22 is provided without the use of silicone oil lubricants. Consequently, the prefilled, sterile syringe 20 of the present invention virtually eliminates the risk of injecting contaminants with the fluids ejected from the syringe.

In another embodiment of a prefilled, sterile delivery apparatus in the form of a syringe indicated generally at 120 in FIG. 2, the piston 132 has a push rod 138 which is configured to engage a recess formed in the piston body. It is also within the scope of the present invention that the piston be gripped and driven by a conventional power injecting device known in the art. As a further variation, the syringe 120 has any suitable means for attaching additional medical apparatus thereto, for example a nut 125 threaded onto nozzle 124 for engaging the conventional luer connector of a catheter (not shown).

The process for producing the prefilled, sterile syringe of the present invention will now be described. The syringe parts, i.e. the container 22, piston 32 and tip seal 26, are first subjected to appropriate steps to wash the same and to remove any debris and contaminants as disclosed in U.S. Patent Nos. 4,628,969 and 4,718,463, assigned to the same assignee as the present application, the subject matter of which patents is incorporated herein by reference. The container 22 is then filled with a desired quantity of fluid material, e.g. contrast media. The piston 32 is then assembled in the open end 28 of the container 22 to seal the liquid in the syringe 20. The assembled syringe 20 and its contents 30 are then sterilized by an appropriate procedure such as being placed in a steam/air autoclave. As also taught in the above patents disclosing methods of producing prefilled, sterile syringes, the steam/air mixture autoclave may selectively add compressed air during the autoclave cycle in order to maintain a pressure on the exterior of the filled syringe which is at least as great as the pressure of the syringe contents.

The present invention provides a prefilled, sterile delivery apparatus having all the attributes of the prior art prefilled, sterile syringes without the disadvantages that arise from the use of silicon oil lubricants. The unexpected discovery that a piston laminated with a solid film lubricant could be used in a prefilled syringe and withstand the extreme conditions that are part of the sterilization process without degradation or delamination of the piston structure provides a superior prefilled, sterile syringe.

It will be understood that many modifications and variations may be made to the present invention described above without departing from the spirit and scope thereof.

What is claimed is:

1. A prefilled, sterilized delivery apparatus comprising:

a container;

two openings formed in said container;

a removable seal on one of said openings to form a sealed opening;

a piston disposed in said container through the other of said openings forming a sealed storage volume within said container;

a volume of fluid stored in said sealed storage volume;

a thin film solid lubricant on an exterior surface of said piston in contact with an inner surface of said container to provide a lubricated sliding interface between the piston and the inner surface of said container; and

wherein the entire prefilled delivery apparatus is sterilized providing a prefilled delivery apparatus having sterile fluid disposed therein.

2. A prefilled, sterilized delivery apparatus as claimed in claim 1, wherein said piston comprises a body portion made of a resilient material and the solid film lubricant is disposed on an exterior surface of said body portion.

3. A prefilled, sterilized delivery apparatus as claimed in claim 1, wherein said solid film lubricant is made of a material selected from the group consisting of tetrafluoroethylene resin, ethylene-tetrafluoroethylene resin, and polyethylene resin.

4. A prefilled, sterilized delivery apparatus as claimed in claim 1, wherein said fluid material is a medical fluid.

5. A method of producing a prefilled, sterilized delivery apparatus containing a sterile fluid therein, the method comprising the steps of:

filling a container having a sealed delivery end with a fluid;

placing a piston having a thin film lubricant on its exterior in an opening in said container opposite said delivery end to seal said fluid within said container; and

subjecting the filled, sealed container to a sterilization process to sterilize the container and fluid contained therein.

6. A method as claimed in claim 5 wherein the step of sterilizing the delivery apparatus is performed by autoclaving.

7. A method as claimed in claim 6 wherein said autoclaving step is performed at a temperature of about 120-125° C.

8. A method as claimed in claim 6 wherein during said autoclaving step, pressure on the outside surface of said container is maintained at least equal to pressure of the interior of said container.

9. A method as claimed in claim 5 wherein the step of filling said container is performed by filling the container with a medical fluid.

10. A method as claimed in claim 5 wherein the step of placing a piston in the container is performed by placing a piston having a body portion whose exterior surface is coated by said solid film lubricant.

11. A method as claimed in claim 5 wherein the step of placing a piston in the container is performed by placing a piston whose exterior surface is coated by a solid film lubricant made of a material selected from the group consisting of tetrafluoroethylene resin, ethylene-tetrafluoroethylene resin, and polyethylene resin.

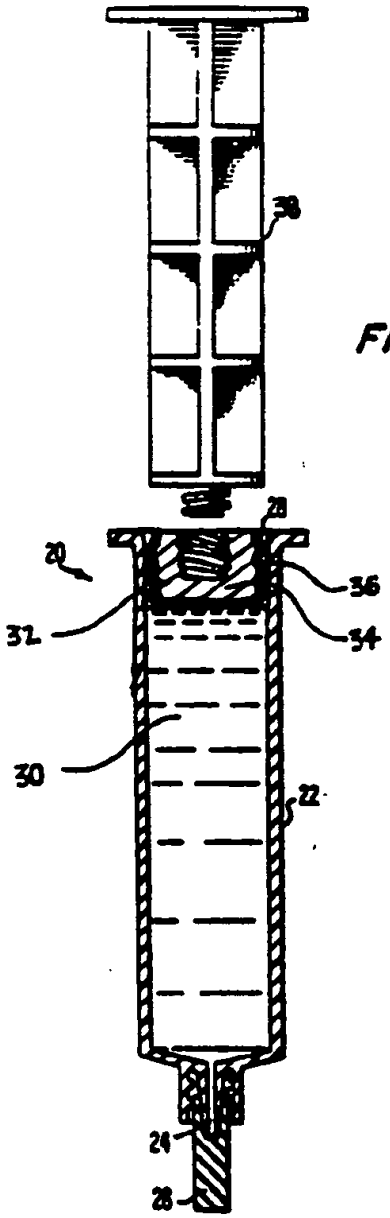

FIG. 1.

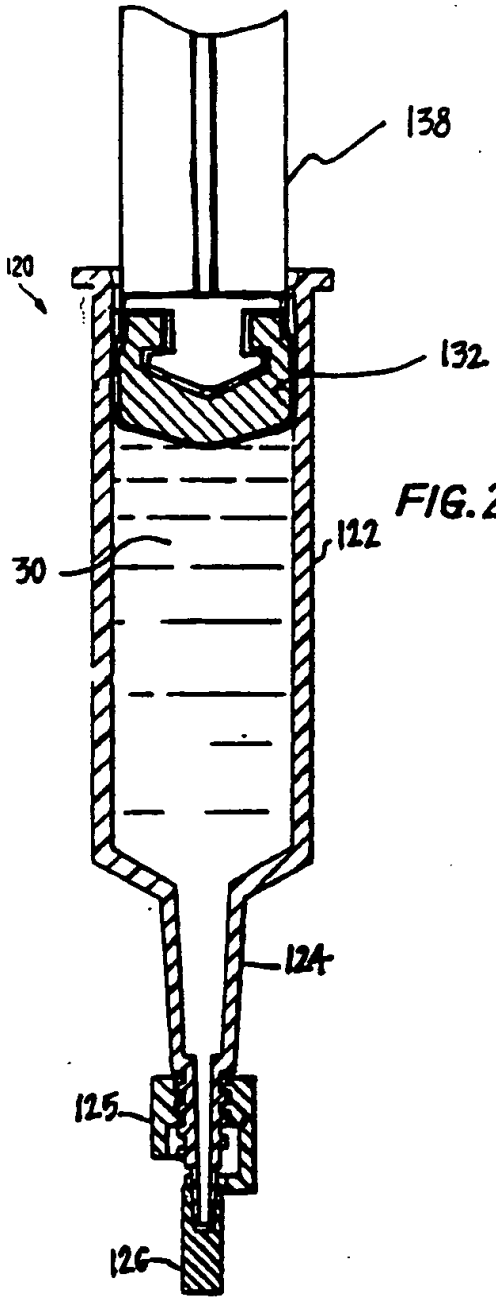

FIG. 2.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/11977

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61M 5/315
US CL :604/218, 230

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/187, 218, 220, 230, 232

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

None

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US, A, 4,997,423, (Okuda et al.), 05 March 1991, see columns 2-4.	1-4 --- 5-11
Y	US, A, 4,718,463, (Jurgens, Jr., et al.), 12 January 1988, see column 4.	5-11

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

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